Analysis of cardiomyocyte clonal expansion during mouse heart development and injury.

Journal: Nat Commun

Publication Year: 2018

Authors: Konstantina-Ioanna Sereti, Ngoc B Nguyen, Paniz Kamran, Peng Zhao, Sara Ranjbarvaziri, Shuin Park, Shan Sabri, James L Engel, Kevin Sung, Rajan P Kulkarni, Yichen Ding, Tzung K Hsiai, Kathrin Plath, Jason Ernst, Debashis Sahoo, Hanna K A Mikkola, M Luisa Iruela-Arispe, Reza Ardehali

PubMed link: 29467410

Funding Grants: Preclinical evaluation of human embryonic stem cell-derived cardiovascular progenitors in a large animal model

Public Summary:
The cellular mechanisms driving cardiac tissue formation remain poorly understood, largely due to the structural and functional complexity of the heart. It is unclear whether newly generated myocytes originate from cardiac stem/progenitor cells or from pre-existing cardiomyocytes that re-enter the cell cycle. Here, we identify the source of new cardiomyocytes during mouse development and after injury. Our findings suggest that cardiac progenitors maintain proliferative potential and are the main source of cardiomyocytes during development; however, the onset of alphaMHC expression leads to reduced cycling capacity. Single-cell RNA sequencing reveals a proliferative, "progenitor-like" population abundant in early embryonic stages that decreases to minimal levels postnatally. Furthermore, cardiac injury by ligation of the left anterior descending artery was found to activate cardiomyocyte proliferation in neonatal but not adult mice. Our data suggest that clonal dominance of differentiating progenitors mediates cardiac development, while a distinct subpopulation of cardiomyocytes may have the potential for limited proliferation during late embryonic development and shortly after birth.

Scientific Abstract:
The cellular mechanisms driving cardiac tissue formation remain poorly understood, largely due to the structural and functional complexity of the heart. It is unclear whether newly generated myocytes originate from cardiac stem/progenitor cells or from pre-existing cardiomyocytes that re-enter the cell cycle. Here, we identify the source of new cardiomyocytes during mouse development and after injury. Our findings suggest that cardiac progenitors maintain proliferative potential and are the main source of cardiomyocytes during development; however, the onset of alphaMHC expression leads to reduced cycling capacity. Single-cell RNA sequencing reveals a proliferative, "progenitor-like" population abundant in early embryonic stages that decreases to minimal levels postnatally. Furthermore, cardiac injury by ligation of the left anterior descending artery was found to activate cardiomyocyte proliferation in neonatal but not adult mice. Our data suggest that clonal dominance of differentiating progenitors mediates cardiac development, while a distinct subpopulation of cardiomyocytes may have the potential for limited proliferation during late embryonic development and shortly after birth.